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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/410,462	10/01/1999	ANGELICA WILLIAMS	ONYX1046-ORD	6889

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

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06/16/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/410,462	WILLIAMS ET AL.	
	Examiner	Art Unit	
	J. E. Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-11,15,17-20,26-28 and 34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *28* is/are allowed.

6)☒ Claim(s) *6,7,11,15,17,18,26 and 27* is/are rejected.

7)☒ Claim(s) *8-10,19,20 and 34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 4/11/2008.

Claims 6-11, 15, 17-20, 26-28 and 34 are currently pending and are addressed herein.

1. In view of the Appeal Brief filed on 2/25/08, PROSECUTION IS HEREBY REOPENED. A new grounds of rejection is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

/JD Schultz, PhD/

Supervisory Patent Examiner, Art Unit 1635.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 6, 7, 11, 15, 17, 18 are rejected under 35 U.S.C. 102(e) as being anticipated by anticipated by U.S. Patent No. 6,080,578 (Bischoff et al., previously of record), for the reasons of record which are reiterated below.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Bischoff et al. teach a cytopathic adenoviral comprising a mutation in an E1A CR2 RB family member binding region as well as methods of using the vector for preferential therapy and prophylaxis of dividing compared to non-dividing cells (e.g., column 3, lines 7-29; column 4, lines 1-55; etc.) Bischoff et al. teach that the mutant adenoviral vector can comprise a mutation can be a e.g., a deletion, substitution frameshift in CR2 domain, amino acids 120-139 (see column 10, lines 10-25). Bischoff specifically teaches a mutant comprising a deletion of amino acids 2-150 (dl 1010) which completely deletes the CR1 and CR2 domains (see column 10, lines 25-40). Bischoff et al. teach that the mutant adenoviral vectors can be used to treat different

types of tumors in a subject by directly administering the vector to the tumor, for instance by swabbing a solution comprising the vector directly on a tumor or by direct injection (e.g., see column 16, lines 26-53). It is noted that patients comprising tumors comprise both dividing cells, such as proliferating cancer cells and proliferating microvascular endothelial cells associated with the tumor, as well as non-dividing non-cancerous cells. For instance, tumors are highly vascularized with blood vessels which are comprised of dividing and non-dividing endothelial cells. Directly administering an adenoviral vector to a tumor would result in administration of the vector to the blood vessels of the tumor. Therefore, administering the vector taught by Bischoff to a subject having a tumor would necessarily result in substantially and selectively killing dividing endothelial cells (including dividing microvasculature) and cancer cells in the subject.

Bischoff et al. teach administering, directly to a tumor, a vector that meets the structural limitations as required by independent claims 11and 15. Applicant is reminded that MPEP § 2112 indicates,

> "[T]he claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)."; and, "There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003)."

Since the adenovirus used in the process taught by Bischoff et al. meets all of the structural limitations of the adenovirus used in the method of the instant claims, it would, absent evidence to the contrary, necessarily have all of the same functions. Thus, the adenovirus would

necessarily replicate to higher titers in dividing endothelial cells than wild-type (non-mutant) adenovirus. It is respectfully pointed out that MPEP § 2112.01 indicates, "'When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.' *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke* 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Furthermore, since the claimed vector and the vector taught by Bischoff are the same structurally, administering the vector taught by Bischoff et al. directly to a tumor would necessarily result in selective killing of dividing endothelial cells relative to killing of quiescent endothelial cells that are present in the tumor mass.

In conclusion, Bischoff et al. anticipates all of the active steps of the claimed methods; therefore, the results of the claimed methods and the methods of Bischoff are inherently the same, regardless if all results were recognized or not in the prior art.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Whyte et al. (J. Virol. 1988, previously of record) in view of U.S. Patent No. 6,080,578 (Bischoff et al., previously of record).

The instant claim is drawn to a composition comprising an Rb binding site adenoviral mutant with a negative selection agent operably linked to a promoter where said adenoviral mutant is dl922/947.

Whyte teaches several mutant adenoviral vectors including the dl922/947 vector (e.g., see Figure 4).

Whyte does not teach that the dl922/947 adenoviral vector comprises a negative selection agent operably linked to a promoter.

Bischoff teaches:

> Although expression of an adenoviral replication phenotype in an infected cell correlates with viral-induced cytotoxicity, generally by cell lysis, cytopathic effect (CPE), apoptosis, or other mechanisms of cell death, it may often be preferable to augment the cytotoxicity of a recombinant adenovirus that is to be used for antineoplastic therapy. Such augmentation may take the form of including a negative selection gene in the recombinant adenovirus, typically operably linked to an adenoviral promoter which exhibits positive transcriptional modulation in cells expressing a replication phenotype. For example, a HSV tk gene cassette may be operably linked immediately downstream of an E3 promoter of a replication deficient adenovirus, such as Ad5 NT dl 1110... Alternatively, a negative selection gene may be operably linked to an adenovirus late region promoter to afford efficient expression of the negative selection gene product in cells expressing a replication phenotype characterized by transcription from late gene promoters.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify dl922/947 adenoviral vector such that it comprised a negative selection agent operably linked to a promoter the with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by Bischoff, who teaches that modifying an adenoviral vector to include a negative selection agent will augment the cytotoxicity of the vector. Therefore, adding the negative selection agent to the vector would result in an adenoviral vector which could be used to as an antineoplastic agent.

4. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Jelsma et al. (Virol. 1989, previously of record) in view of U.S. Patent No. 6,080,578 (Bischoff et al., previously of record).

The instant claim is drawn to a composition comprising an Rb binding site adenoviral mutant with a negative selection agent operably linked to a promoter where said adenoviral mutant is dl1107.

Jelsma several mutant adenoviral vectors including the dl1107 vector (e.g., see Figure 1).

Jelsma does not teach that the dl1107 adenoviral vector comprises a negative selection agent operably linked to a promoter.

Bischoff teaches:

> Although expression of an adenoviral replication phenotype in an infected cell correlates with viral-induced cytotoxicity, generally by cell lysis, cytopathic effect (CPE), apoptosis, or other mechanisms of cell death, it may often be preferable to augment the cytotoxicity of a recombinant adenovirus that is to be used for antineoplastic therapy. Such augmentation may take the form of including a negative selection gene in the recombinant adenovirus, typically operably linked to an adenoviral promoter which exhibits positive transcriptional modulation in cells expressing a replication phenotype. For example, a HSV tk gene cassette may be operably linked immediately downstream of an E3 promoter of a replication deficient adenovirus, such as Ad5 NT dl1110... Alternatively, a negative selection gene may be operably linked to an adenovirus late region promoter to afford efficient expression of the negative selection gene product in cells expressing a replication phenotype characterized by transcription from late gene promoters.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify dl1107 adenoviral vector such that it comprised a negative selection agent operably linked to a promoter the with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by Bischoff, who teaches that modifying an adenoviral vector to include a negative selection agent will augment the cytotoxicity of the vector. Therefore, adding the negative selection agent to the vector would result in an adenoviral vector which could be used to as an antineoplastic agent.

Allowable Subject Matter

Claim 28 is allowed.

5. Claims 8-10, 19, 20, 34 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Applicants' arguments in the Appeal Brief filed 2/25/08 are acknowledged. It is noted, however, that the instant action contains new grounds of rejection which are not addressed in the arguments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. E. Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m. .

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/
Primary Examiner, Art Unit 1635